

CLAIMS

What is claimed is:

1. A method for identifying a test compound as a candidate for an antibiotic, comprising:
 - a) contacting a PBG polypeptide with a test compound; and
 - b) detecting the presence or absence of binding between the test compound and the PBG polypeptide, wherein binding indicates that the test compound is a candidate for an antibiotic.
2. The method of claim 1, wherein the PBG polypeptide is a fungal PBG polypeptide.
3. The method of claim 1, wherein the PBG polypeptide is a *Magnaporthe* PBG polypeptide.
4. The method of claim 1, wherein the PBG polypeptide is SEQ ID NO:3.
5. A method for identifying a test compound as a candidate for an antibiotic, comprising:
 - a) contacting a test compound with a polypeptide selected from the group consisting of:
 - i) a polypeptide consisting essentially of SEQ ID NO:3;
 - ii) a polypeptide having at least ten consecutive amino acids of SEQ ID NO:3;
 - iii) a polypeptide having at least 42% sequence identity with SEQ ID NO:3 and at least 10% of the activity of SEQ ID NO:3; and
 - iv) a polypeptide consisting of at least 50 amino acids having at least 42% sequence identity with SEQ ID NO:3 and at least 10% of the activity of SEQ ID NO:3; and
 - b) detecting the presence and/or absence of binding between the test compound and the polypeptide, wherein binding indicates that the test compound is a candidate for an antibiotic.
6. A method for identifying a test compound as a candidate for an antibiotic, comprising:

- a) contacting porphobilinogen and H₂O with a PBG in the presence and absence of a test compound or contacting hydroxymethylbilane and NH₃ with a PBG in the presence and absence of a test compound; and
 - b) determining a change in concentration for at least one of porphobilinogen, H₂O hydroxymethylbilane and/or NH₃ in the presence and absence of the test compound, wherein a change in the concentration for any of porphobilinogen, H₂O hydroxymethylbilane and/or NH₃ indicates that the test compound is a candidate for an antibiotic.
7. The method of claim 6, wherein the PBG is a fungal PBG.
 8. The method of claim 7, wherein the PBG is a *Magnaporthe* PBG.
 9. The method of claim 8, wherein the PBG is SEQ ID NO:3.
 10. A method for identifying a test compound as a candidate for an antibiotic, comprising:
 - a) contacting a PBG polypeptide with porphobilinogen and H₂O in the presence and absence of a test compound or with hydroxymethylbilane and NH₃ in the presence and absence of a test compound, wherein the PBG polypeptide is selected from the group consisting of:
 - i) a polypeptide having at least 42% sequence identity with SEQ ID NO:3 and at least 10% of the activity of SEQ ID NO:3,
 - ii) a polypeptide consisting essentially of SEQ ID NO:3,
 - iii) a polypeptide comprising at least 50 consecutive amino acids of SEQ ID NO:3 and having at least 10% of the activity of SEQ ID NO:3; and
 - iv) a polypeptide consisting of at least 50 amino acids having at least 42% sequence identity with SEQ ID NO:3 and having at least 10% of the activity of SEQ ID NO:3; and
 - b) determining a change in concentration for at least one of porphobilinogen, H₂O, hydroxymethylbilane and/or NH₃ in the presence and absence of the test compound,

wherein a change in the concentration for any of porphobilinogen, H₂O, hydroxymethylbilane and/or NH₃ indicates that the test compound is a candidate for an antibiotic.

11. A method for identifying a test compound as a candidate for an antibiotic, comprising:
 - a) measuring the expression of a PBG in an organism, or a cell or tissue thereof, in the presence and absence of a test compound; and
 - b) comparing the expression of the PBG in the presence and absence of the test compound, wherein an altered expression in the presence of the test compound indicates that the test compound is a candidate for an antibiotic.
12. The method of claim 11, wherein the organism is a fungus.
13. The method of claim 12, wherein the organism is *Magnaporthe*.
14. The method of claim 11, wherein the PBG is SEQ ID NO:3.
15. The method of claim 11, wherein the expression of the PBG is measured by detecting the PBG mRNA.
16. The method of claim 11, wherein the expression of the PBG is measured by detecting the PBG polypeptide.
17. The method of claim 11, wherein the expression of the PBG is measured by detecting the PBG polypeptide enzyme activity.
18. A method for identifying a test compound as a candidate for an antibiotic, comprising:
 - a) providing a fungal organism having a first form of a PBG;

- b) providing a fungal organism having a second form of the PBG, wherein one of the first or the second form of the PBG has at least 10% of the activity of SEQ ID NO:3; and
 - c) determining the growth of the organism having the first form of the PBG and the organism having the second form of the PBG in the presence of a test compound, wherein a difference in growth between the two organisms in the presence of the test compound indicates that the test compound is a candidate for an antibiotic.
19. The method of claim 18, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe* and the first and the second form of the PBG are fungal PBG's.
20. The method of claim 18, wherein the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2.
21. The method of claim 18, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe* and the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2.
22. The method of claim 18, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe*, the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2, and the second form of the PBG is a heterologous PBG.
23. The method of claim 18, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe*, the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2, and the second form of the PBG is SEQ ID NO:1 or SEQ ID NO:2 comprising a transposon insertion that reduces or abolishes PBG activity.

24. A method for identifying a test compound as a candidate for an antibiotic, comprising:
- a) providing a fungal organism having a first form of a PBG;
 - b) providing a fungal organism having a second form of the PBG, wherein one of the first or the second form of the PBG has at least 10% of the activity of SEQ ID NO:3; and
 - c) determining the pathogenicity of the organism having the first form of the PBG and the organism having the second form of the PBG in the presence of a test compound,
- wherein a difference in pathogenicity between the two organisms in the presence of the test compound indicates that the test compound is a candidate for an antibiotic.
25. The method of claim 24, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe* and the first and the second form of the PBG are fungal PBG's.
26. The method of claim 24, wherein the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2.
27. The method of claim 24, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe* and the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2.
28. The method of claim 24, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe*, the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2, and the second form of the PBG is a heterologous PBG.
29. The method of claim 24, wherein the fungal organism having the first form of the PBG and the fungal organism having the second form of the PBG are *Magnaporthe*, the first form of the PBG is SEQ ID NO:1 or SEQ ID NO:2, and the second form of

the PBG is SEQ ID NO:1 or SEQ ID NO:2 comprising a transposon insertion that reduces or abolishes PBG activity.

30. A method for identifying a test compound as a candidate for an antibiotic, comprising:

- a) providing a fungal organism having a first form of a gene in the heme biosynthetic pathway;
- b) providing a fungal organism having a second form of said gene in the heme biosynthetic pathway, wherein one of the first or the second form of the gene has at least 10% of the activity of a corresponding *Magnaporthe grisea* gene; and
- c) determining the growth of the organism having the first form of the gene and the organism having the second form of the gene in the presence of a test compound,

wherein a difference in growth between the two organisms in the presence of the test compound indicates that the test compound is a candidate for an antibiotic.

31. The method of claim 30, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*.

32. The method of claim 30, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe* porphobilinogen synthase, and the second form of the gene is a heterologous porphobilinogen synthase.

33. The method of claim 30, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* porphobilinogen synthase, and the second form of the gene is *Magnaporthe grisea*

porphobilinogen synthase comprising a transposon insertion that reduces or abolishes porphobilinogen synthase protein activity.

34. The method of claim 30, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* uroporphyrinogen-III synthase, and the second form of the gene is a heterologous uroporphyrinogen-III synthase.
35. The method of claim 30, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* uroporphyrinogen-III synthase, and the second form of the gene is *Magnaporthe grisea* uroporphyrinogen-III synthase comprising a transposon insertion that reduces or abolishes uroporphyrinogen-III synthase protein activity.
36. A method for identifying a test compound as a candidate for an antibiotic, comprising:
- a) providing a fungal organism having a first form of a gene in the heme biosynthetic pathway;
 - b) providing a fungal organism having a second form of said gene in the heme biosynthetic pathway, wherein one of the first or the second form of the gene has at least 10% of the activity of a corresponding *Magnaporthe grisea* gene; and
 - c) determining the pathogenicity of the organism having the first form of the gene and the organism having the second form of the gene in the presence of a test compound,
- wherein a difference in pathogenicity between the organism and the comparison organism in the presence of the test compound indicates that the test compound is a candidate for an antibiotic.

37. The method of claim 36, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*.
38. The method of claim 36, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* porphobilinogen synthase, and the second form of the gene is a heterologous porphobilinogen synthase.
39. The method of claim 36, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* porphobilinogen synthase, and the second form of the gene is *Magnaporthe grisea* porphobilinogen synthase comprising a transposon insertion that reduces or abolishes porphobilinogen synthase protein activity.
40. The method of claim 36, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of the gene in the heme biosynthetic pathway is *Magnaporthe grisea* uroporphyrinogen-III synthase, and the second form of the gene is a heterologous uroporphyrinogen-III synthase.
41. The method of claim 36, wherein the fungal organism having the first form of the gene and the fungal organism having the second form of the gene are *Magnaporthe*, the first form of a gene in the heme biosynthetic pathway is *Magnaporthe grisea* uroporphyrinogen-III synthase, and the second form of the gene is *Magnaporthe grisea* uroporphyrinogen-III synthase comprising a transposon insertion that reduces or abolishes uroporphyrinogen-III synthase protein activity.
42. A method for identifying a test compound as a candidate for an antibiotic, comprising:

- a) providing paired growth media containing a test compound, wherein the paired growth media comprise a first medium and a second medium and the second medium contains a higher level of heme than the first medium;
- b) inoculating the first and the second medium with an organism; and
- c) determining the growth of the organism, wherein a difference in growth of the organism between the first and second medium indicates that the test compound is a candidate for an antibiotic.

43. The method of claim 42, wherein the organism is a fungus.

44. The method of claim 42, wherein the organism is *Magnaporthe*.

45. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide of SEQ ID NO:3.

46. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide having at least 42% sequence identity to SEQ ID NO:3 and having at least 10% of the activity of SEQ ID NO:3.

47. An isolated nucleic acid comprising a nucleotide sequence that encodes a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO:3.

48. A polypeptide consisting essentially of the amino acid sequence of SEQ ID NO:3.

49. A polypeptide comprising the amino acid sequence of SEQ ID NO:3.